REMARKS

Claims 8-10, 13, 14, and 16-36 have been withdrawn, as drawn to the non-elected invention. Claims 1-7, 11, 12 and 15 are currently under examination in the present application. Claims 1-6, 11 and 12 have been rejected and claims 7 and 15 have been objected to. Claim 1 has been amended. No new matter has been added. Applicants reserve the right to refile this subject matter in a continuation or divisional application filed during the pendency of this application.

Specification Objections

The title of the invention was objected to as not descriptive of the invention, and for the recitation of "novel." Applicants have amended the title to more accurately describe the present invention, thereby obviating the objection. Withdrawal of the objection is respectively requested.

The abstract was objected to as it was entitled" Abstract of the Invention." Applicants have amended the abstract to be entitled "Abstract," thereby obviating the objection. Withdrawal of the objection is respectively requested.

Rejection under 35 U.S.C. § 102(a)

Claims 1-3 were rejected under 35 U.S.C. § 102 (a) as being anticipated by Martinez et al. The instant claims are drawn to a gene expression modulation system wherein the first gene expression vector comprises a DBD and an LBD; and a second gene expression vector which comprises a transactivation domain and LBD not from USP. The examiner suggests that these claims are anticipated by Martinez et al. because the reference teaches an inducible gene expression system comprising three vectors, the first comprises the GR DBD and EcR LBD, the second comprises the VP16 transactivation domain and the EcR LBD, and the third comprises a response element, promoter and reporter gene.

Applicants contend that Martinez et al. actually teach a two vector inducible gene expression system, not a three vector system as suggested. Martinez et al. describe and teach an inducible system that comprises only one LBD. Martinez et al. describe on page 548 in Figure 1 the various constructs made in order to examine their

individual abilities to induce reporter gene (β-glucuronidase) expression (GUS). The constructs are as follows:

1) a full-length glucocorticoid receptor GR (**GR**)
2) the transactivation domain (AD) and DBD of GR fused to the hinge domain and LBD of *Dm*EcR (**GRD**)
3) the transactivation domain (AD) and DBD of GR fused to the hinge domain and LBD of *Hv*EcR (**GRH**), or
4) the GRH vector in which a portion of the GR sequence was replaced with a VP16AD (**GRvH**).

On page 549, Martinez et al. describe the co-transformation of **individual** effector constructs (1, 2, 3 **or** 4 from above) with a reporter plasmid, and the evaluation of each in transactivation assays. Figures 2, 3, 4 and 6 depict the ability of each **individual** effector construct to cause the transcriptional activation of GUS. Figure 2 depicts the transcriptional activation of GUS by GR. GR vector was co-transformed with reporter plasmid into maize protoplasts and then incubated with dexamethasone or muristerone A, and activity of GUS analyzed. Figure 3 depicts the transcriptional activation of GUS by GRD **or** GRH. GRH **or** GRD was co-transformed with reporter plasmid into maize protoplasts and then incubated with or without RH-5992, and activity of GUS analyzed. Figure 4 depicts the transcriptional activation of GUS by GRH. GRH was co-transformed with reporter plasmid into maize protoplasts and then incubated with or without RH-5992, and activity of GUS analyzed. Figure 6 depicts the transcriptional activation of GUS by GRvH. GRvH was co-transformed with reporter plasmid into maize protoplasts and then incubated with or without RH-5992, and activity of GUS analyzed.

Applicants submit that the present invention is an inducible gene expression system which comprises a **first vector** comprising a DBD and LBD from a nuclear receptor and a **second vector** comprising an AD and LBD from a nuclear receptor other than USP. The third vector of the present invention comprises a response element, promoter and gene to be expressed. Martinez et al. teach only a **first vector** comprising an AD, DBD and LBD, and a second reporter vector.

Martinez et al. fail to teach or disclose Applicants' invention. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V.*

Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d, 1913, 1920 (Fed. Cir. 1989). The prior art fails to provide each and every element set forth in the present claims for the reasons set forth above.

Thus, Applicants maintain that the cited prior art fails to teach or disclose the present invention as required to set forth anticipation of the claims. Accordingly, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1-6, 11 and 12 were rejected under 35 U.S.C. § 103(a) as unpatentable over Martinez et al. in view of Gage et al. (U.S. 5,919,667). The instant claims are drawn to a gene expression modulation system wherein the first gene expression vector comprises a DBD and an LBD, wherein the LBD is an ecdysone receptor; and a second gene expression vector which comprises a transactivation domain and LBD not from USP. The examiner suggests that these claims are unpatentable because the Martinez et al. reference teaches an inducible gene expression system comprising three vectors, the first comprises GR DBD and EcR LBD and the second comprises VP16 AD and EcR LBD; and the third is a reporter gene construct. The examiner does submit that the Martinez et al. reference does not teach the gene expression system wherein the second LBD is from RXR. However, the examiner implies that the '667 patent discloses a transgenic animal that contains one or more expression constructs containing nucleic acid encoding an EcR, exogenous RXR and a heterologous gene under the transcription control of an EcR response element, and therefore it would have been obvious to one of skill in the art to make a gene expression modulation system where the first gene expression vector comprises a DBD and an LBD, wherein the LBD is an ecdysone receptor; and a second gene expression vector which comprises a transactivation domain and LBD not from USP.

To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). For the reasons previously presented above, Applicants contend that Martinez et al. **do not teach** an inducible gene expression system comprising three vectors, the first comprising GR DBD and EcR LBD, the second

comprising VP16 AD and EcR LBD, and the third comprising a reporter gene. Martinez et al. do not teach or even suggest a second receptor (LBD) vector. Martinez et al. teach an inducible gene expression system comprising:

1) a full-length glucocorticoid receptor GR (**GR**);

2) the transactivation domain (AD) and DBD of GR fused to the hinge domain and LBD of *Dm*EcR (**GRD**);

3) the transactivation domain (AD) and DBD of GR fused to the hinge domain and LBD of *Hv*EcR (**GRH**), **or**

5) the GRH vector in which a portion of the GR sequence was replaced with a VP16AD (**GRvH**).

Martinez et al. do not teach or suggest all the claim limitations of the present invention, and thus do not support a *prima facie* case of obviousness.

Gage et al. teach a MARV vector which can comprise a receptor complex of EcR and RXR, and a MARSHA vector which comprises the gene to be expressed and the response element. Gage et al. does not teach an inducible gene expression system which comprises a **first vector** comprising a DBD and LBD from a nuclear receptor and a **second vector** comprising an AD and LBD from a nuclear receptor other than USP. As Martinez et al. do not teach the use of a second LBD or receptor partner, one of skill in the art would not be motivated to combine these references. Furthermore, Martinez et al. provide no suggestion of using or even needing a second LBD. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). In the case of Martinez et al. there is no use or desirability in using a second LBD, and therefore no desirability or motivation to combine those teachings with the teachings of Gage et al.

In view of the foregoing amendments and remarks, Applicants submit that this application is in condition for allowance. Therefore, Applicants respectfully request reconsideration and withdrawal of all of the above rejections.

Respectfully submitted,

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